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Review

RECIST revisited: A review of validation studies on tumour assessment

P. Therasse, E.A. Eisenhauer, J. Verweij*

EORTC Data center, Avenue E. Mounier, 83 Box 11, 1200 Brussels, Belgium

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ABSTRACT

The response evaluation criteria in solid tumours (RECIST) was developed in the late 1990s to replace the WHO criteria for response evaluation. The new criteria included important changes such as unidimensional tumour measurement, selection of target lesions with a minimum size, details concerning imaging modalities and a new threshold for assignment of objective progression.

RECIST was published in February 2000 and very quickly came into operation first in clinical trials performed under the auspices of EORTC, US NCI or NCI Canada Clinical Trials Group but was adopted quickly thereafter by the entire cancer clinical research community. As several key features of RECIST were based on analysis of retrospective clinical data, it was felt important to carefully monitor the implementation of the guidelines and stimulate prospective validation studies. This paper reviews the literature that has been published on RECIST from 2000 up to November 2005. In total 60 papers and ASCO, abstracts directly refer to research studies or reviews related to RECIST and its implementation. Amongst the 60 references identified for this review, 11 papers refer to validation studies (seven prospective and four retrospective), six papers refer to the comparison of unidimensional measurements versus bi or tri-dimensional measurements, 12 papers address issues raised with the implementation of RECIST in Mesothelioma and Gastro-Intestinal Stromal Tumours and four papers report on an adaptation of RECIST for specific tumour types.

In general, RECIST has been well received by the scientific community and most validation studies fully support the implementation of the new criteria. As expected, however, some issues have been identified. In keeping with the mathematical differences in definition of progression, RECIST delays the identification of progression as compared to WHO criteria in some instances. RECIST criteria are not easily applicable in some types of trials such as those in paediatric tumours and in mesothelioma. Furthermore, anatomical changes in the tumour as described by RECIST may be detected later than functional changes in some circumstances, as for example in Gastro-Intestinal Stromal Tumours treated with Imatinib. However, there is no other universal method of tumour assessment as yet and functional imaging methods have not been validated and will not be widely available for some time. The findings of this review, together with experience acquired thus far and the results of some ongoing research projects, have paved the way for RECIST 2.0 to be hopefully announced later this year.

* *Corresponding author:* Tel.: +32 2 774 16 14; fax: +32 2 772 61 97.
E-mail address: patrick.therasse@eortc.be (P. Therasse).
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1. Introduction

Response evaluation criteria in solid tumours (RECIST) was introduced by a small international working group in February 2000 to facilitate, improve and standardize the evaluation and the reporting of objective tumour outcomes in early clinical trials investigating new anti-cancer agents.[1] In comparison to earlier response assessment systems, the new criteria gave much more detailed recommendations on how to assess tumour lesions, how to report responses, and also took into account recent developments in medical imaging techniques. RECIST uses a unidimensional measure (the longest diameter) to quantify measurable tumour lesions as opposed to the bidimensional product (longest diameter multiplied by its perpendicular), which was commonly employed by earlier iterations of response criteria.[2–4] Building on the work of others,[3,5] RECIST defines measurable lesions as those with a minimum size depending on the method of investigation. Following a principle already implemented in the SWOG response criteria,[3] the threshold for defining objective progression was arbitrarily increased as compared to the WHO criteria, i.e., the increase in measurable overall tumour burden required for progression was greater in RECIST (20% in one dimension being approximately equivalent to a 44% increase in bidimensional product) than in the WHO criteria (25% increase in product).

Following the publication of RECIST, standard case report forms (CRFs) and protocol sections were created by the working group and made available on the web. A special email address was created to receive and answer questions related to the implementation of the criteria. A website was created to host the Questions and Answers to facilitate the implementation of the criteria (www.eortc.be\recist). Although the last comment on the website was posted in 2003, the RECIST working group continues (weekly) to answer questions and provide support for the interpretation of the criteria in specific situations.

After the publication of RECIST, some investigators raised concerns about the interest, the pertinence and the applicability of the new criteria. The main purpose of this paper is to review the work performed and published by other colleagues on the usefulness of the criteria in general and their validation in specific tumour types when available.

2. Review methodology

The search strategy was simple and made through PUBMED using the word RECIST as keyword to identify titles and abstracts published between February 2000 and November 2005. This search strategy identified 99 referenced papers. Only those manuscripts reporting on original work focused on the methodology of response evaluation and RECIST were retained for detailed review. Also excluded were editorial comments and non-English literature. Ultimately 43 papers satisfied these criteria. A second search was undertaken of abstracts published in the American Society of Clinical Oncology (ASCO) annual conference proceedings between 2001 and 2005. This identified a further nine abstracts (and related data in oral presentations or posters) that had not yet been followed by a full paper. Finally, examination of the reference lists in the 43 full papers yielded another eight additional papers which met the review criteria. Thus in total, 60 studies (51 papers and nine ASCO abstracts) were identified for inclusion in this review.

3. Results

The studies included focused either on general principles relating to the implementation of RECIST (or tumour evaluation) or on a prospective or retrospective attempt to validate the utility of RECIST in certain tumour types. Accordingly, the results of this review have been divided into general and tumour specific considerations.

3.1. *General considerations*

One of the first papers to refer to RECIST was a commentary of Padhani and Husband.[6] The authors outlined the problems inherent to the morphological assessments of tumours independently of the number of dimensions being measured and briefly explored the development of functional imaging as a tool for the future. However, their conclusion was crystal clear: “current criteria should remain unchallenged until better functional parameters emerge”. One year later the same first author[7] analysed RECIST and its impact on radiology departments highlighting the possibility that the implementation of RECIST could translate into increased workload. The paper concluded that, while the issue of workload required careful monitoring, this factor alone should not be an argument to be less stringent in response assessment in the performance of clinical trials. Institutions that could not provide this service should be considered incapable of performing studies where response assessment is crucial. In 2004, the International Cancer Imaging Society (ICIS) published a consensus statement about the evaluation of the response to treatment of solid tumours,[8] including a number of issues related to the implementation of RECIST (Table 1). Another paper[9] published almost simultaneously but in another journal identified very similar issues. It is interesting to note that on one hand these authors cite concern about the potential increase in workload created with the application of RECIST (specifically the requirement to measure up to 10 lesions if multiple measurable lesions are identified), while on the other hand advise consideration for the use of 3D measurements. Three dimensional measurements to date have not been shown to be more useful than 1D measurements (for the purpose of response evaluation), but is certainly much more complex and time consuming.

The general concordance between RECIST and WHO criteria was tested retrospectively in a cohort of 130 patients with different tumour types and entered into different protocols.[10] In line with the larger increase in lesion size required for definition of progressive disease (PD) found in RECIST , it was shown that about 1/3 of patients normally identified as PD with WHO criteria would still be classified as having stable disease (SD) with RECIST. The authors also used this dataset to create multiple simulations to artificially change tumour shape to demonstrate that increasing the irregularity of lesions may decrease the concordance rate of partial response (PR) and SD categories between the two methods.